

Please amend the application as follows:

IN THE CLAIMS

1. (currently amended) A replication-competent adenovirus vector for selective cytolysis of a target cell comprising,

a hypoxia responsive element (HRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4, wherein said HRE comprises a binding site for hypoxia inducible factor-1; and in a target cell wherein said hypoxia inducible factor-1 is present, said adenovirus vector results in selective cytolysis due to selective replication in said target cell.

2-7. (canceled)

8. (previously presented) The adenovirus vector of claim 1, wherein the HRE is human.

9-13. (canceled)

14. (previously presented) The adenovirus vector of claim 1, wherein said adenovirus gene essential for replication is operably linked to a composite regulatory element comprising said HRE and a tumor cell-specific transcriptional regulatory element (TRE).

15. (previously presented) The adenovirus vector of claim 14, wherein said tumor cell-specific TRE comprises a promoter.

16. (previously presented) The adenovirus vector of claim 14, wherein said tumor cell-specific TRE comprises an enhancer.

17-20. (canceled)

21. (previously presented) The adenovirus vector of claim 14, wherein said tumor cell-specific TRE comprises a prostate specific promoter and enhancer.

22-23. (canceled)

24. (previously presented) A composition comprising:  
a replication-competent adenovirus vector of claim 1 and a pharmaceutically acceptable excipient.

25. (previously presented) An isolated host cell comprising the adenovirus vector of claim 1.

26. (previously presented) A method of propagating adenovirus *in vitro*, the method comprising:

introducing into a cell an adenovirus vector comprising a hypoxia responsive element (HRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4, wherein said HRE comprises a binding site for hypoxia inducible factor-1 wherein said cell is maintained under hypoxic conditions *in vitro*, thereby expressing said adenovirus gene essential for replication;

wherein said adenovirus is propagated.

27-31. (canceled)

32. (previously presented) The method of Claim 26, wherein said propagating of said adenovirus is cytotoxic to said cell.

33. (previously presented) The method of Claim 32, wherein said cell is a tumor cell.

34. (previously presented) The adenovirus vector of claim 14, wherein said tumor cell-specific transcriptional regulatory element (TRE) is selected from the group consisting of a prostate-specific TRE (PSA-TRE), a glandular kallikrein-1 TRE (*hKLK2*-TRE), a probasin TRE (*PB*-TRE), an  $\alpha$ -fetoprotein TRE (AFP TRE) and a carcinoembryonic antigen TRE (CEA TRE).

35. (currently amended) A replication-competent adenovirus vector for selective cytolysis of a target cell, comprising:

an E2F-1 transcriptional regulatory element (TRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4, wherein and in a target cell wherein RB function is disrupted, said adenovirus vector results in selective cytolysis due to selective replication ~~in said target cell~~.

36. (previously presented) The adenovirus vector of claim 35, wherein the E2F-1 TRE is human.

37. (previously presented) The adenovirus vector of Claim 36, wherein said E2F-1 TRE comprises the nucleotide sequence set forth in SEQ ID NO:2.

38. (previously presented) The adenovirus vector of Claim 35, wherein said E2F-1 TRE comprises a nucleotide sequence having at least 80% sequence identity with the sequence set forth in SEQ ID NO:2.

39. (previously presented) The adenovirus vector of Claim 35, wherein said E2F-1 TRE comprises a nucleotide sequence that hybridizes under stringent conditions with the sequence set forth in SEQ ID NO:2.

40. (currently amended) The adenovirus vector of Claim 35, wherein said adenovirus gene essential for replication is operably linked to a composite regulatory element comprising said HRE E2F-1 transcriptional regulatory element and a cell-type specific transcriptional regulatory element (TRE).

41. (previously presented) The adenovirus vector of claim 40, wherein said tumor cell-specific transcriptional regulatory element (TRE) is selected from the group consisting of a prostate-specific TRE (PSA-TRE), a glandular kallikrein-1 TRE (*hKLK2*-TRE), a probasin TRE (*PB*-TRE), an  $\alpha$ -fetoprotein TRE (AFP TRE) and a carcinoembryonic antigen TRE (CEA TRE).

42. (previously presented) A composition comprising:  
a replication competent adenovirus vector of claim 35 and a pharmaceutically acceptable excipient.

43. (previously presented) An isolated host cell comprising the adenovirus vector of Claim 35.

44. (previously presented) A method of propagating adenovirus *in vitro*, the method comprising:

a replication competent adenovirus vector for selective cytolysis of a target cell, comprising an E2F-1 transcriptional regulatory element (TRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4 wherein said cell is maintained under cell cycling conditions *in vitro*, thereby expressing said adenovirus gene essential for replication;

wherein said adenovirus is propagated.

45. (previously presented) The method of Claim 44, wherein said propagating of said adenovirus is cytotoxic to said cell.

46. (previously presented) The method of Claim 44, wherein said cell is a tumor cell.

47. (new) A replication-competent adenovirus vector for selective cytolysis of a target cell comprising,

a hypoxia responsive element (HRE) comprising a binding site for hypoxia inducible factor-1 operably linked to a first adenovirus gene essential for replication and a transcriptional regulatory element (TRE) comprising a heterologous promoter or enhancer operably linked to a second adenoviral gene essential for replication wherein said first and second adenoviral genes essential for replication are selected from the group consisting of E1A, E1B and E4; and in a target cell wherein said hypoxia inducible factor-1 is present, said adenovirus vector results in cytolysis due to selective replication.

48. (new) The replication-competent adenovirus vector of claim 47, wherein said transcriptional regulatory element (TRE) linked to said second adenoviral gene essential for replication is a cell status-specific transcriptional regulatory element (TRE).

49. (new) The replication-competent adenovirus vector of claim 47, wherein said transcriptional regulatory element (TRE) linked to said second adenoviral gene essential for replication is a cell type-specific transcriptional regulatory element (TRE).

50. (new) A replication-competent adenovirus vector for selective cytolysis of a target cell, comprising:

an E2F-1 transcriptional regulatory element (TRE) operably linked to a first adenovirus gene essential for replication and a transcriptional regulatory element (TRE) comprising a heterologous

promoter or enhancer operably linked to a second adenoviral gene essential for replication wherein said first and second adenoviral genes essential for replication are selected from the group consisting of E1A, E1B and E4; and in a target cell wherein RB function is disrupted, said adenovirus vector results in cytolysis due to selective replication.

51. (new) The replication-competent adenovirus vector of claim 50, wherein said transcriptional regulatory element (TRE) linked to said second adenoviral gene essential for replication is a cell status-specific transcriptional regulatory element (TRE).

52. (new) The replication-competent adenovirus vector of claim 50, wherein said transcriptional regulatory element (TRE) linked to said second adenoviral gene essential for replication is a cell type-specific transcriptional regulatory element (TRE).

53. (new) A replication-competent adenovirus vector for selective cytolysis of a target cell comprising,

a hypoxia responsive element (HRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4, wherein said HRE comprises a binding site for hypoxia inducible factor-1; and in tumor target cell, said adenovirus vector results in cytolysis due to selective replication.

54. (new) A replication-competent adenovirus vector for selective cytolysis of a target cell, comprising:

an E2F-1 transcriptional regulatory element (TRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4, and in a tumor target cell, said adenovirus vector results in cytolysis due to selective replication.